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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,891	03/31/2006	Tatsuo Hoshino	21421 US C038435/0185661	4642

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EXAMINER	
FRONDA, CHRISTIAN L	
ART UNIT	**PAPER NUMBER**
1652	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/528,891	HOSHINO ET AL.	
	Examiner	Art Unit	
	Christian L. Fronda	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-8 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-8 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 3/23/05.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-8 are pending and under consideration in this Office Action.

2. The disclosure is objected to because of the following informality: in the specification there is no statement that indicates that the instant application is the US National Stage filing of PCT Application No. PCT/EP03/10403, filed 09/18/2003, which claims foreign priority under 35 U.S.C. 119(a) (d) to foreign patent application EPO 02021623.0 filed 09/27/2002. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. Appropriate correction is required.

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR §§ 1.821 through 1.825 for the following reason(s): a paper copy of the Sequence Listing has not been received. Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (1) a recombinant *E.coli* host transformed with plasmids comprising a polynucleotide encoding erythrose 4-phosphate dehydrogenase obtained from *E.coli* chromosomal DNA by PCR using primers of SEQ ID NO: 1 and SEQ ID NO: 2, a polynucleotide encoding 1-deoxy-D-xylulose-5-phosphate synthase obtained from *E.coli* chromosomal DNA by PCR using primers of SEQ ID NO: 5 and SEQ ID NO: 6, and a polynucleotide encoding pyridoxol 5'-phosphate synthase obtained from *E.coli* chromosomal DNA by PCR using primers of SEQ ID NO: 9 and SEQ ID NO: 10, where said recombinant *E.coli* host overproduces vitamin B6 compared to an untransformed *E.coli* host, and (2) a process for preparing vitamin B6 comprising culturing said recombinant *E.coli* host; does not reasonably provide enablement for any other embodiment as recited in the claims. The specification does

not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized In re Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claims encompass any recombinant microorganism capable of producing vitamin B6 which carries extra genes coding for any erythrose 4-phosphate dehydrogenase, any 1-deoxy-D-xylulose-5-phosphate synthase, and any pyridoxol 5'-phosphate synthase, where the genes and enzymes are from any biological source for which no structure and amino acid or nucleotide sequence is apparent, and any process for preparing vitamin B6 using said recombinant microorganism.

The specification provides guidance and working examples for a recombinant *E.coli* host (AT1024/pKK-epd/pVK-pdxJ/pSTV-dxs) transformed with plasmids comprising a polynucleotide encoding erythrose 4-phosphate dehydrogenase obtained from *E.coli* chromosomal DNA by PCR using primers of SEQ ID NO: 1 and SEQ ID NO: 2, a polynucleotide encoding 1-deoxy-D-xylulose-5-phosphate synthase obtained from *E.coli* chromosomal DNA by PCR using primers of SEQ ID NO: 5 and SEQ ID NO: 6, and a polynucleotide encoding pyridoxol 5'-phosphate synthase obtained from *E.coli* chromosomal DNA by PCR using primers of SEQ ID NO: 9 and SEQ ID NO: 10, where said recombinant *E.coli* host overproduces vitamin B6 compared to an untransformed *E.coli* host, and a process for preparing vitamin B6 comprising culturing said recombinant *E.coli* host.

However, the specification does not provide guidance, working examples, or prediction for making any recombinant microorganism capable of producing vitamin B6 which carries extra genes coding for any erythrose 4-phosphate dehydrogenase, any 1-deoxy-D-xylulose-5-phosphate synthase, and any pyridoxol 5'-phosphate synthase, where the genes and enzymes are from any biological source for which no structure and amino acid or nucleotide sequence is apparent, and any process for preparing vitamin B6 using said recombinant microorganism.

Thus, an undue amount of trial and error experimentation must be preformed where such experimentation involves searching and screening a vast number of biological sources for any gene encoding any erythrose 4-phosphate dehydrogenase, any 1-deoxy-D-xylulose-5-phosphate synthase, and any pyridoxol 5'-phosphate synthase; transforming the genes into any recombinant microorganism; and determining if the transformed recombinant microorganism can produce vitamin B6. General teaching regarding screening and searching for the claimed invention is not guidance for making the claimed invention.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in

the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, such as information regarding the specific SEQ ID NOs of the polynucleotides encoding erythrose 4-phosphate dehydrogenase, 1-deoxy-D-xylulose-5-phosphate synthase, and pyridoxol 5'-phosphate synthase, the experimentation left to those skilled in the art to make and/or use the claimed invention is unnecessarily, and improperly, extensive and undue.

6. Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a genus of recombinant microorganisms comprising a genus of erythrose 4-phosphate dehydrogenases, a genus of 1-deoxy-D-xylulose-5-phosphate synthases, and a genus of pyridoxol 5'-phosphate synthases for which no structure and amino acid or nucleotide sequence is apparent. The scope of the each genus includes many members with widely differing structural, chemical, and physiochemical properties including widely differing amino acid sequences, structures, and biological functions. Furthermore, each genus is highly variable because a significant number of structural and biological differences between genus members exist.

The specification discloses a recombinant *E.coli* host AT1024/pKK-epd/pVK-pdxJ/pSTV-dxs transformed with plasmids comprising a polynucleotide encoding erythrose 4-phosphate dehydrogenase obtained from *E.coli* chromosomal DNA by PCR using primers of SEQ ID NO: 1 and SEQ ID NO: 2, a polynucleotide encoding 1-deoxy-D-xylulose-5-phosphate synthase obtained from *E.coli* chromosomal DNA by PCR using primers of SEQ ID NO: 5 and SEQ ID NO: 6, and a polynucleotide encoding pyridoxol 5'-phosphate synthase obtained from *E.coli* chromosomal DNA by PCR using primers of SEQ ID NO: 9 and SEQ ID NO: 10, where said recombinant *E.coli* host overproduces vitamin B6 compared to an untransformed *E.coli* host, and a process for preparing vitamin B6 comprising culturing said recombinant *E.coli* host AT1024/pKK-epd/pVK-pdxJ/pSTV-dxs.

However, the specification does not describe and define any structural features, amino acid sequences, and biological functions that are commonly possessed by members of the each genus. The specification fails to provide a written description of additional recombinant microorganisms being capable of producing vitamin B6. The above stated recombinant *E.coli* host AT1024/pKK-epd/pVK-pdxJ/pSTV-dxs is insufficient to be representative of the attributes and features common to all the members of each claimed genus. Thus, one skilled in the art cannot visualize or recognize the identity of the members of each genus.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definitions, such as the structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v, Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997), quoting *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe the genus of genetic materials, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g. structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these. Therefore, the instant claims are not adequately described.

In view of the above considerations, one of skill in the art would not recognize that applicants were in possession of the claimed genus of recombinant microorganisms and process for producing vitamin B6 using the claimed genus of recombinant microorganisms.

Furthermore, the claims encompass any genes encoding any erythrose 4-phosphate dehydrogenase, any genus of 1-deoxy-D-xylulose-5-phosphate synthases, and any pyridoxol 5'-phosphate synthases. Gene elements which are not particularly described, including promoter regions, regulatory elements, and untranslated regions, are essential to the function of the claimed invention since the claims recite the term "gene". The art indicates that the structure of these gene elements are empirically determined. Therefore, the structure of these elements which applicants considers as being essential to the function of the claim are not conventional in the art.

There is no known or disclosed correlation between the coding region of a polynucleotide encoding a polypeptide or enzyme and the structure of the non-described promoter regions, regulatory elements, and untranslated regions. In view of the above considerations, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize applicants were in possession of any genes encoding any erythrose 4-phosphate dehydrogenase, any genus of 1-deoxy-D-xylulose-5-phosphate synthases, and any pyridoxol 5'-phosphate synthases.

Conclusion

7. No claim is allowed.

8. The following reference made of record and not relied upon is considered pertinent to applicant's disclosure: Tazoe et al. (J Bacteriol. 2006 Jul;188(13):4635-45) teach that flavin adenine dinucleotide-dependent 4-phospho-D-erythronate dehydrogenase is responsible for the 4-phosphohydroxy-L-threonine pathway in vitamin B6 biosynthesis in *Sinorhizobium meliloti*.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

10. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CLF

TEKCHAND SAIDHA 2/2/07
PRIMARY EXAMINER